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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|--|-------------|----------------------|---------------------|------------------|
| 09/763,370 | 02/21/2001 | Etsuro Ogata | OGATA4 | 9907 |
| 1444 | 7590 | 11/17/2005 | EXAMINER | |
| BROWDY AND NEIMARK, P.L.L.C. 624 NINTH STREET, NW SUITE 300 WASHINGTON, DC 20001-5303 | | | HARRIS, ALANA M | |
| | | ART UNIT | PAPER NUMBER | |
| | | 1643 | | |

DATE MAILED: 11/17/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

| | | |
|------------------------------|------------------------------------|------------------|
| Office Action Summary | Application No. | Applicant(s) |
| | 09/763,370 | OGATA ET AL. |
| | Examiner Alana M. Harris, Ph.D. | Art Unit 1643 |

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) Responsive to communication(s) filed on 08/25/05.
- 2a) This action is **FINAL**. 2b) This action is non-final.
- 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) Claim(s) 2-6,8-15 and 25-30 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) Claim(s) _____ is/are allowed.
- 6) Claim(s) 2-6,8-15 and 25-30 is/are rejected.
- 7) Claim(s) _____ is/are objected to.
- 8) Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) The specification is objected to by the Examiner.
- 10) The drawing(s) filed on _____ is/are: a) accepted or b) objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) All b) Some * c) None of:
 1. Certified copies of the priority documents have been received.
 2. Certified copies of the priority documents have been received in Application No. _____.
 3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) Notice of References Cited (PTO-892)
- 2) Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____.
- 4) Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____.
- 5) Notice of Informal Patent Application (PTO-152)
- 6) Other: _____.

DETAILED ACTION

Response to Amendments and Arguments

1. Claims 2-6 and 8-15 are pending.

Claims 6, 8-11, 14 and 15 have been amended.

Claims 16, 17, 20 and 21 have been cancelled.

Claims 25-30 have been added.

Claims 2-6, 8-15 and 25-30 are examined on the merits.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Withdrawn Rejections

Claim Rejections - 35 USC § 112

3. The rejection of claims 2-6 and 8-15 under 35 U.S.C. 112, first paragraph, set forth in the Action mailed February 25, 2005 as failing to comply with the written description requirement is withdrawn in light of Applicants' amendments. Claims 20 and 21 have been cancelled.

4. The rejection of claims 2-6 and 12-15, sections a and c under 35 U.S.C. 112, second paragraph, presented in the Action mailed February 25, 2005 as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant

regards as the invention is withdrawn in light of Applicants' amendments and cancellation of claims. Claims 16, 17, 20 and 21 have been cancelled.

Claim Rejections - 35 USC § 102

5. The rejection of claims 2-6 under 35 U.S.C. 102(b) as being anticipated by Koizumi et al. (J. Cancer Res. Clin. Oncol. 121: 542-548, 1995) is withdrawn in light of the claim amendments, namely the introduction of the Z value and crossover index algorithms.
6. The rejection of claims 8-15 under 35 U.S.C. 102(b) as being anticipated by Martinetti et al. Tumor Biol. 18: 197-205, 1997) is withdrawn in light of the claim amendments, namely the introduction of the Z value and crossover index algorithms.

Maintained Rejections

Claim Rejections - 35 USC § 112

7. The rejection of claims 2-6, 8-15 and 25-30 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is maintained and made. Claims 16, 17, 20 and 21 have been cancelled.

- a. Claim 6 is vague and indefinite because the preamble reads on using two markers, one that reflects the activity of osteoblasts and the other reflects the activity of osteoclasts, however the method comprises testing blood for a marker of metabolism,

this being just one marker. The method further includes testing comprising measuring both osteocalcin and one marker from the group selected from BALP, PICP and PINP, which are all bone formation markers just like osteocalcin. The steps are incongruent with the preamble and moreover do not provide information as to how amelioration and or exacerbation of metastasis is assessed. The preamble addresses both osteoclast and osteoblast activity, but the method steps only provide for measuring osteoblast activity.

b. Claims 6, 8 and 30 are vague and indefinite in the recitation "and determining a crossover index by dividing said Z value for osteocalcin by said Z value for ..., said crossover index providing a diagnosis...". This recitation is not clear in yielding information such as a particular number means for example drugs are effective or bone metastasis has progressed.

c. Claim 6 recites an improper Markush group, "...one marker selected from BALP, PICP and PINP.". Applicants are advised to reformat the claim to read "...one marker selected from the group consisting of BALP, PICP and PINP."

d. Claims 8-17 continue to be vague and indefinite because it is not clear from the claims how the two markers are used in ascertaining efficacy of a drug and the method steps are not clear. Likewise, is the case for claims 2-6 and 25-30. Applicants simply note that the comments presented in rebuttal to the 112, first paragraph rejection should be applied herein, see Remarks submitted August 25, 2005, page 12, first paragraph.

While the claims note that one marker represents osteoclast activity and the other is for osteoblast activity it not clear how the Z values obtained from the markers relate to the efficacy of the drug used in cancer treatment. Furthermore, it is not noted in the claims that a particular number obtained from the Z value means the drugs are effective or not. The claims seems to be remiss of a wherein clause further detailing if a certain number is obtained for the Z value it means this opposed to that.

Independent claim 6 has now been amended to include determining a Z value, however neither the claims, nor its dependent claims establish what a Z value means in regard diagnosing amelioration and/or exacerbation. Applicants are requested to discriminately review all claims and ensure clarity and completeness.

e. Claim 8 is vague and indefinite because the claim notes in the preamble that the evaluation of efficacy of drugs is based on assessing one marker of osteoblast activity or one marker of osteoclast marker. However, steps 1 and 2 reflect that both said markers are to be assessed. The steps are not commensurate with the preamble. Furthermore, testing involves just assessing one marker of bone metabolism from the patient, then the steps listed on page 6, lines 1-3 require measuring two of four bone formation markers. The method steps seem to involve just assessing bone formation markers and not involving bone resorption markers.

f. Claim 8, line 18 lack antecedent bases for the recitation "said patient".

g. The recitation "...measuring for both osteocalcin and for BALP, PICP or PINP..." in claim 30, line 7 is vague and indefinite. It is not clear what two markers of

the four listed are to be measured. Accordingly, the metes and bounds cannot be determined.

Conclusion

8. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

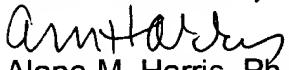
A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Alana M. Harris, Ph.D. whose telephone number is (571)272-0831. The examiner works a flexible schedule, however she can normally be reached between the hours of 7:30 am to 6:30 pm with alternate Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry R. Helms can be reached on (571) 272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

ALANA M. HARRIS, PH.D.
PRIMARY EXAMINER


Alana M. Harris, Ph.D.
14 November 2005